

REMARKS

Upon entry of present amendment, claims 1, 2, 4-7, 10, 12, 13, 30-39, and 44-69 will be pending. Claims 1, 2, 4, 13, 30-34, and 44-69 are currently under examination. Claims 1 and 32-34 have been amended without prejudice to future prosecution to recite methods comprising administering a pharmaceutical composition consisting essentially of 1-methyl-D-tryptophan. Support for amended claims 1 and 32-34 can be found in the specification as filed, *e.g.*, at page 2, lines 29-31, at page 15, lines 1-8, and in original claim 11. Claim 13 has been amended without prejudice to further prosecution to recite additional types of cancer. Support for amended claim 13 can be found in the specification as filed, *e.g.*, at page 16, lines 7-16. Claim 2 has been amended to reflect proper formalities. Claims 9 and 11 have been cancelled by the present amendment.

New claims 44-69 have been added. Support for new claims can be found throughout the specification, as filed. For example, support for claims 44-48 can be found in the specification at page 2, lines 12-15 and lines 29-31, and in original claims 1, 3, 11, and 12. Support for claims 49-53 can be found in original claim 34 and in the specification at page 2, lines 29-31. Support for claims 54, 68, and 69 can be found in original claim 4 and in the specification at page 15, lines 18-22. Support for new claims 55 and 56 can be found in the original claim 13 and in the specification at page 17, lines 13-21. Support for claims 57 and 58 can be found in original claims 30 and 31 and in the specification at page 15, lines 14-16 and lines 22-27. Support for claims 59 and 65 can be found in the specification at page 16, lines 25-30 through page 17, lines 1-2. Support for claim 60 can be found on page 18, lines 28-31 of the specification. Support for claims 61-64 can be found in the specification, on page 19, lines 12-18. Support for claim 66 can be found in the specification on page 19, lines 23-24. Support for claim 67 can be found in the

specification on page 16, lines 20-21 and on page 15, lines 13-18.

Applicants submit that no prohibited new matter has been added.

Consideration of the amended and the new claims is respectfully required.

Information Disclosure Statement

Applicants note with appreciation consideration of the references listed with the Information Disclosure Statement mailed on April 14, 2008. Applicants request that the Examiner further consider and return a marked copy of the 1449 form listing references filed with the Information Disclosure Statement on July 9, 2008.

Claim Numbering

As an initial matter and to obtain a clear record, Applicants note the following regarding claim numbering in the present application. Claims 1-43 were pending in the originally-filed application. Claims 38-43 (among others) were cancelled in an amendment filed on mailed on January 19, 2007. New claims 38 and 39 were added in an amendment mailed on September 28, 2007, and were subsequently examined. Present amendment begins new claims at number 44 to follow previously-cancelled claims.

Rejections under 35 U.S.C. § 102(e)

The Examiner has rejected claims 1, 2, 4, 9, 11, 13, and 32-34 as allegedly being anticipated by Prendergast *et al.*, WO 2004/09387 ("Prendergast") (Office Action at page 3). Without conceding to the substance of the rejection, but solely in the interest of expediting allowance of the claimed subject matter, independent claims 1 and 32-34 have been amended to recite methods that comprise administering a pharmaceutical composition consisting essentially of **1-methyl-D-tryptophan** (D1MT). Reconsideration

and withdrawal of the rejection under 102(e) are respectfully requested.

Rejections under 35 U.S.C. § 103(a)

The Examiner has rejected claims 30 and 31 as allegedly being rendered obvious by Prendergast (Office Action at page 4). Applicants respectfully disagree with the rejection. Nonetheless, solely in the interest of expediting allowance of the pending claims, Applicants amended the claims as discussed above. Reconsideration and withdrawal of the rejection under 103(a) based on Prendergast are respectfully requested.

Claims 1, 2, 4, 9, 11, 13, and 30-34 have been rejected as allegedly obvious over WO 00/66764 ("van den Eynde") and Tsung *et al.*, *J. Immunol.* 16:1369-77, 1998 ("Tsung") in view of Pinedo *et al.*, *The Oncologists* 5:497-500, 2000 ("Pinedo") (Office Action at page 5). Applicants respectfully disagree with the rejection. Nevertheless, the present claims have been amended as discussed *supra* in order to expedite allowance. Applicants submit that van den Eynde, Tsung, and Pinedo do not, individually or in combination, teach administering to the subject: (a) a pharmaceutical composition consisting essentially of **1-methyl-D-tryptophan**, (b) a pharmaceutical composition comprising **1-methyl-D-tryptophan**, but not 1-methyl-(D,L)-tryptophan, or (c) a pharmaceutical composition comprising **1-methyl-D-tryptophan**, but not 1-methyl-L-tryptophan. Thus, because the references do not teach all elements of the new or amended claims, they do not render obvious the pending claims.

Applicants also submit that D1MT exhibits different structural and functional properties than a racemic mixture comprising both the L and the D stereoisomers or the L stereoisomer alone. In fact, prior art **teaches away** from use of D1MT as an IDO inhibitor. For example, Peterson *et al.* (*Med. Chem. Res.* 3:531-44, 1994; submitted with Information Disclosure Statement filed September 28, 2007 (considered by

Examiner on December 6, 2007), courtesy copy submitted herewith as Exhibit C), shows that the L isomer is “significantly more active” than the D isomer (at page 531; see also Table 1 at page 536). In contrast to prior art, Applicants have unexpectedly found that D1MT is more effective than the L isomer at reversing IDO-mediated suppression (specification at page 51, lines 7-8) and more effective than the racemic mixture in delaying tumor growth (specification at page 53, lines 12-14). Neither van den Eynde nor Tsung nor Pinedo makes up for the general teaching away of the art from the use of D1MT. It is a well-settled principle that prior art must be considered in its entirety, including disclosures that teach away from the claims (see *KSR Int'l. Co. v. Teleflex, Inc.*, 127 S.Ct. 1727; *Gore & Associates, Inc. v. Garlock*, 721 F.2d 1540 (Fed. Cir. 1983); and MPEP § 2141.02 VI.).

The Examiner has acknowledged that Applicants have shown unexpected results for the treatment of melanoma with cyclophosphamide and 1-MT, but not for the broader scope of the claims, which includes treatment of **any** cancer with **any** cytotoxic antineoplastic agent in combination with 1-MT (Office Action at page 10). In this regard, Applicants show a synergistic effect of 1-methyl-D-tryptophan (D-1MT) in an *in vivo* cancer model with **both** radiation and chemotherapeutic agents (see pages 52-53 of the specification). Given these results, and the fact that radiation and chemotherapy act by different mechanisms in cancer treatment, one of skill in the art would fully expect D-1MT to find use in a wide array of cancer treatment regimens in conjunction with a wide array of different therapies, including various types of chemotherapeutic agents.

Further, Applicants submit herewith Declaration under 37 C.F.R. §1.132 of Dr. George C. Prendergast, which includes data showing that administration of D-1MT as part of a treatment regimen also including administration of a chemotherapeutic agent resulted in the inhibition of two other types of tumor cells: **lung** cancer cells and **colon**

cancer cells. Therefore, one skilled in the art would be able to utilize the present invention in a wide variety of cancers, as the methods of the present invention have broad applicability.

Reconsideration and withdrawal of this 103(a) rejection are respectfully requested.

Double Patenting

The Examiner has provisionally rejected claims 1-4, 9, 11, 13, 30, and 31 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6-10 and 17-26 of copending Application No. 10/780,150 (Office Action at page 11). Claims 9 and 11 have been cancelled by the present amendment. Applicants respectfully request that this rejection be held in abeyance until indication of otherwise allowable subject matter, and Applicants will consider at that time whether the submission of a terminal disclaimer would be appropriate.

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SUMMARY

Applicants respectfully submit that the claims are now in condition for allowance, early notice of which would be appreciated. Should the Examiner disagree, Applicants respectfully request a telephonic or in-person interview with the undersigned attorney to discuss any remaining issues and to expedite the eventual allowance of the claims.

The Examiner is invited to contact Applicants' Representatives at the telephone number listed below if they can be of any assistance during prosecution of the present application.

CERTIFICATE UNDER 37 C.F.R.1.8:

The undersigned hereby certifies that this paper is being transmitted via the U.S. Patent and Trademark Office electronic filing system in accordance with 37 CFR §1.6(a)(4) to the Patent and Trademark Office addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 14 day of October, 2008.

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